ABSTRACT OF THE DISCLOSURE

The present invention provides methods for identifying improved folate antagonists. The improved folate antagonists identified by the methods of the invention have increased selectivity. The increased selectivity of the folate antagonists results in a reduced risk of adverse effects following treatment with the improved folate antagonists. The improved folate antagonists are identified based on their reduced binding affinity for at least one enzyme selected from glutathione synthase, pyruvate carboxylase, propionyl-CoA carboxylase, biotin carboxylase, acetyl-CoA carboxylase, and methylcrotonyl-CoA carboxylase. According to the invention, folate antagonists having reduced affinity for at least one enzyme selected from this group of enzymes are selected for the treatment of neoplastic, hyperproliferative, and immune disorders.